

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for preparing a 6-oxo-14-hydroxy- Δ^7 -morphinane comprising oxidising a 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane for a time and under conditions sufficient to form
5 a 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane-N-oxide and converting the formed N-oxide to the 6-oxo-14-hydroxy- Δ^7 -morphinane.
2. A method according to claim 1 wherein the oxidation is carried out by treating the 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane with hydrogen peroxide in the presence of a
10 carboxylic acid.
3. A method according to claim 2 wherein the carboxylic acid is formic acid or acetic acid.
- 15 4. A method according to claim 3 wherein the carboxylic acid is formic acid.
5. A method according to claim 4 wherein the concentration of formic acid is 45% by weight formic acid in water.
- 20 6. A method according to any one of claims 2 to 5 wherein the 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane is treated with a molar excess of hydrogen peroxide at a concentration of 50% by weight in water.
7. A method according to any one of claims 2 to 6 wherein the 6-methoxy-N-methyl-
25 Δ^6, Δ^8 -morphinane is dissolved in a mixture of the carboxylic acid and a solvent prior to the addition of the hydrogen peroxide.
8. A method according to claim 7 wherein the solvent is ethanol.
- 30 9. A method according to any one of claims 1 to 8 wherein the oxidation is conducted at a temperature below 50°C.

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10. A method according to claim 9 wherein the temperature is about 20°C.
11. A method according to any one of claims 1 to 10 including the additional step of
5 isolating the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinan-N-oxide before the conversion to 6-oxo-14-hydroxy- Δ^7 -morphinan.
12. A method according to claim 11 wherein the isolation step comprises neutralising
10 the oxidation reaction mixture to a pH of about 7 by adding a base and collecting the N-oxide as a solid.
13. A method according to claim 12 wherein the base is selected from sodium or potassium hydroxide or potassium carbonate.
- 15 14. A method according to claim 13 wherein the base is sodium hydroxide.
15. A method according to claim 14 wherein sodium hydroxide is added to the
oxidation reaction mixture at a rate which ensures that the reaction temperature reaches
20 55°C.
16. A method according to any one of claims 1 to 15 wherein the formed N-oxide is converted to the 6-oxo-14-hydroxy- Δ^7 -morphine by treating the N-oxide with a reducing agent.
- 25 17. A method for converting a 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinan-N-oxide to a 6-oxo-14-hydroxy- Δ^7 -morphinan comprising subjecting the N-oxide to reducing conditions to ring close the N-methyl group with the 14-hydroxy group forming an oxazolidine ring, and hydrolysing the ring closed oxazolidine product to form the 6-oxo-14-hydroxy- Δ^7 -morphinan.
- 30 18. A method according to claim 17 wherein the reducing conditions comprise treating

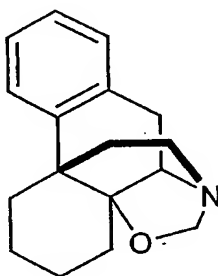
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the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane-N-oxide with a Fe(II) based reducing agent and formic acid.

19. A method according to claim 17 wherein the hydrolysing step is performed using a strong acid selected from hydrochloric acid, sulphuric acid, hydrobromic acid or phosphoric acid.

20. A method according to claim 19 wherein the strong acid is hydrochloric acid.

21. A method of preparing a morphinane compound having a modified morphinane skeleton of structure (B)



(B)

15 said method comprising treating a 6-oxo-N-methyl-14-hydroxy- Δ^7 -morphinane-N-oxide with an Fe(II) reducing agent for a time and under conditions sufficient to ring close the N-methyl group with the 14-hydroxy group.

22. A method according to claim 19 wherein the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane-N-oxide is treated as a slurry in methanol with a Fe(II) based reducing agent, whereby formic acid is added.

23. A method according to claim 21 or 22 wherein the Fe(II) reducing agent is FeSO₄.

24. A method for preparing N-alkyl or N-alkenyl 6-oxo-14-hydroxy-morphinanes comprising:

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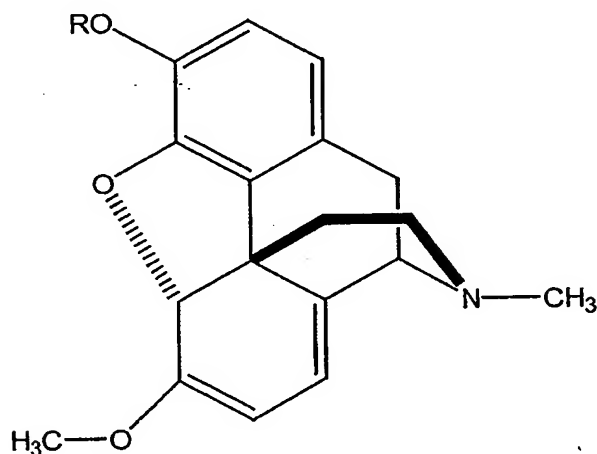
oxidising a 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane for a time and under conditions sufficient to form a 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane-N-oxide,

5 converting the formed N-oxide to a 6-oxo-14-hydroxy- Δ^7 -morphinane,

reducing the Δ^7 double bond to form a 6-oxo-14-hydroxy morphinane, and

10 subjecting the 6-oxo-14-hydroxy-morphinane to N-alkylation to introduce the N-alkyl or N-alkenyl substituent.

25. A method according to any one of claims 1 to 16 and 24 wherein the 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane is a compound of formula I:



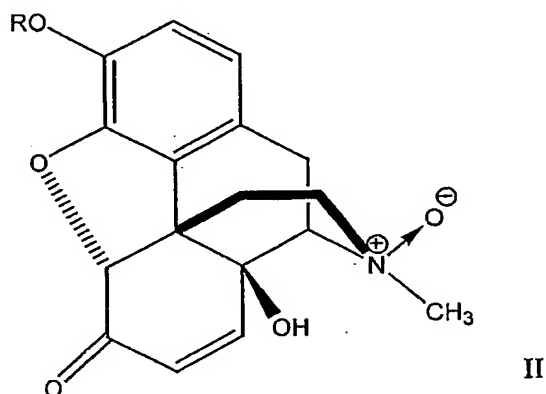
where R is H, C₁-C₆ alkyl, benzyl or acyl.

26. A method according to claim 25 wherein the 6-methoxy-N-methyl- Δ^6, Δ^8 -
20 morphinane is a compound of formula I where R is H or CH₃.

27. A method according to claim 25 wherein wherein the 6-methoxy-N-methyl- Δ^6, Δ^8 -morphinane is a compound of formula I where R is H.

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28. A method according to any one of claims 1 to 24 wherein the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane-N-oxide is compound of formula II:



where R is independently selected from H, C₁-C₆alkyl, benzyl or acyl.

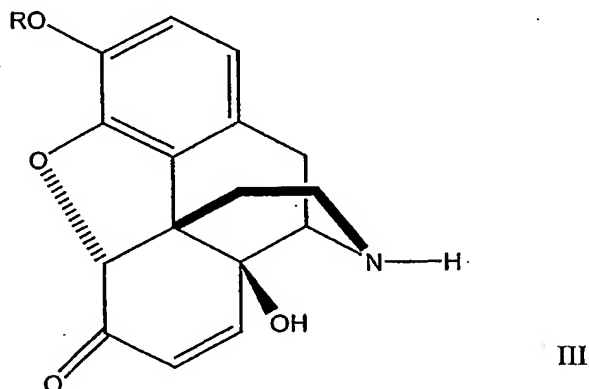
29. A method according to claim 28 wherein the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane N-oxide is compound of formula II where R is H or CH₃.

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30. A method according to claim 29 wherein the 6-oxo-14-hydroxy-N-methyl- Δ^7 -morphinane N-oxide is a compound of formula II where R is H.

31. A method according to any one of claims 1 to 20 and 24 wherein the 6-oxo-14-hydroxy- Δ^7 -morphinane is a compound of formula III:

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wherein R is H, C₁-C₆alkyl, benzyl or acyl.

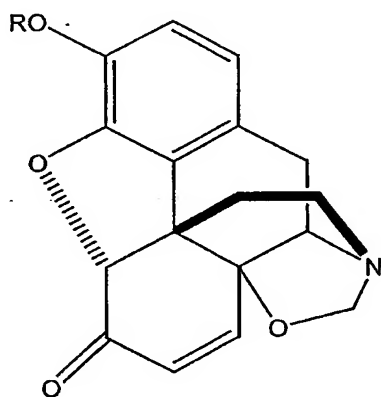
32. A method according to claim 31 wherein the 6-oxo-14-hydroxy- Δ^7 -morphinane is a compound of formula III where R is H or CH₃.

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33. A method according to claim 32 wherein the 6-oxo-14-hydroxy- Δ^7 -morphinane is a compound of formula III where R is H.

34. An oxazolidine of formula IV:

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IV

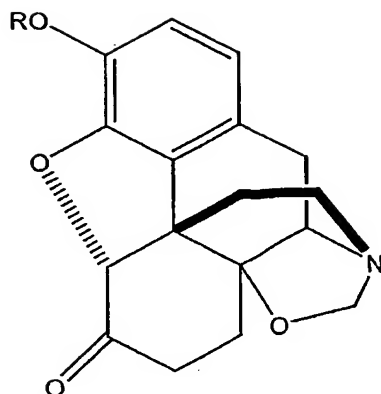
where R is H, C₁-C₆alkyl, benzyl or acyl.

15 35. An oxazolidine of formula IV according to claim 34 wherein R is H, CH₃ or benzyl.

36. An oxazolidine of formula IV according to claim 35 wherein R is H.

20 37. An oxazolidine of formula V:

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V

where R is H, C₁-C₆alkyl, benzyl or acyl.

5 38. An oxazolidine of formula V according to claim 37 wherein R is H or CH₃.

39. An oxazolidine of formula V according to claim 38 wherein R is H.

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